work by Baillard et al. In fact, later work by Dubois et al. has evaluated the repeatability of paired train-of-four ratio determinations, and their results showed much less variability of acceleromyography measurements. Most investigators agree that if high stimulating currents (50 to 60 mA) are used, best practice may be to test patients in the operating room during anesthesia and to check for adequate recovery before emergence from anesthesia, assuring patient comfort.

Residual Neuromuscular Blockade and Quantitative Monitoring

We wholeheartedly agree with Drs. Phillips and Stewart that the proper use of quantitative monitoring will help improve the quality of patient care by decreasing the incidence of postoperative residual blockade. In a recent article, we clearly stated our position and addressed the current challenges facing the implementation of routine objective monitoring.8 We do, however, disagree with Drs. Phillips and Stewart in their statement that the results of Murphy et al.'s study do not support the conclusion; we believe the results are clear. We have attempted to point out that neostigmine, administered during near-complete recovery from nondepolarizing neuromuscular block (not in the absence of a neuromuscular blocking drug), will not induce paradoxical neuromuscular weakness. Murphy et al. have settled this controversy, and clinicians owe them a debt of gratitude. We would be remiss, however, if we did not reiterate our warnings and recommendations that we have made for the past three decades—and that are identical to those of Drs. Phillips and Stewart: “To improve the safety of reversal, routine use of quantitative monitoring will help guide the selection of most appropriate reversal agent and to confirm adequacy of reversal should be mandatory.”

Competing Interests

Dr. Brull has intellectual property assigned to Mayo Clinic (Rochester, Minnesota); has received research funding from Merck & Co., Inc. (Kenilworth, New Jersey; funds to Mayo Clinic); is a principal and shareholder in Senzime AB (publ; Uppsala, Sweden); and is a member of the Scientific Advisory Boards for ClearLine MD (Woburn, Massachusetts); The Doctors Company (Napa, California), and NMD Pharma (Aarhus, Denmark). Dr. Naguib has served as a consultant for GE Healthcare (Chicago, Illinois) in 2018.


References

1. Murphy GS, Szokol JW, Avram MJ, Greenberg SB, Shear TD, Deshur MA, Benson J, Newmark RL, Maher CE: Neostigmine administration after spontaneous recovery to a train-of-four ratio of 0.9 to 1.0: A randomized controlled trial of the effect on neuromuscular and clinical recovery. Anesthesiology 2018; 128:27–37

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In Reply:

We thank Drs. Phillips and Stewart for their interest in our article.1 The effect of neostigmine when given at the time neuromuscular recovery remains controversial, and Drs. Phillips and Stewart raise some important questions. We welcome the opportunity to respond to their queries.

We agree that we did not determine whether neostigmine induced depolarizing neuromuscular blockade. In order to assess this outcome measure, single twitch height must be recorded before and after muscle relaxant administration. In our clinical trial, we objectively evaluated muscle strength recovery by determining train-of-four ratios.1 No patient exhibited evidence of neostigmine-induced muscle weakness, as train-of-four ratios did not decrease in any subject. Both quantitative techniques (single twitch height and train-of-four ratios) are effective in objectively measuring muscle strength, and further studies are needed to assess the effect of neostigmine on single twitch height.

We also agree that standard clinical tests of signs of muscle weakness (5-s head lift) are unreliable in determining the presence of full neuromuscular recovery.2 However, we have previously determined that symptoms of muscle weakness (subjective feeling of difficulty performing the 5-s head lift) may be present when all clinical signs suggest full neuromuscular recovery has occurred, and may be more predictive of incomplete recovery.3,4 In our investigation, more symptoms of muscle weakness were present in the group randomized to receive saline, compared to neostigmine, which suggests that neostigmine did not produce clinical evidence of muscle weakness. We hypothesize that the reason that all patients were able to perform the 5-s head lift before extubation, and nine patients were unable to complete the test after

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admission to the recovery room, was related to the stimulation of an endotracheal tube at the time of extubation.

The peak effect of the neostigmine occurs 5 to 10 min after administration. This typically corresponds to the time of tracheal extubation. It would not be possible to conduct a comprehensive examination of patients for signs and symptoms of muscle weakness immediately before or after the removal of the endotracheal tube. This assessment was performed 15 min after postanesthesia care unit (PACU) admission, at a time when patients were sufficiently awake to cooperate with the research team. Given the duration of effect of neostigmine (typically 40 min or longer), we would likely have observed neostigmine-induced muscle weakness, if it were present, in the PACU. In contrast, patients who were administered neostigmine exhibited fewer symptoms of impaired neuromuscular recovery, compared to the control group. Furthermore, patients were carefully examined for any evidence of airway obstruction or hypoxic events from the time of tracheal extubation until 30 min after PACU arrival. No clinical evidence of an adverse effect of neostigmine on airway function was observed. In fact, the incidence of hypoxic events in the PACU was twice as high in the control-saline group.

Acceleromyography may recover slightly earlier than electromyography or mechanomyography. However, standalone electromyography and mechanomyography are no longer commercially manufactured, and acceleromyography is now considered the “gold standard” for clinical trials. As Drs. Phillips and Stewart note, some patients may have received neostigmine before full neuromuscular recovery had occurred, as documented with acceleromyography. However, many likely recovered hours before neostigmine was administered, since a small dose of rocuronium was given for induction and none thereafter; no clinical evidence of neostigmine-induced muscle weakness was observed in any of these subjects. In addition, as the authors note, two acceleromyography measurements made in the PACU may be discordant in awake patients; however, most of our acceleromyography assessments were performed in patients before emergence, and those measured in the PACU that differed by more than 10% were not recorded.

In our clinical investigation, with a careful examination of patients for adverse respiratory events and a thorough assessment for signs and symptoms of incomplete neuromuscular recovery, we were unable to detect any evidence of neostigmine-induced muscle weakness. Given the relatively high incidence of residual neuromuscular blockade observed in our study (21%), despite the low doses of rocuronium administered (25 mg) and long duration of cases (163 min), we believe our findings support the routine use of reversal agents, unless quantitative monitoring is used.

Competing Interests

Dr. Murphy has received speaking fees and has served on the advisory board for Merck (Kenilworth, New Jersey). The remaining authors declare no competing interests.

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References

1. Murphy GS, Szokol JW, Avram MJ, Greenberg SB, Shear TD, Deshur MA, Benson J, Newmark RL, Maher CE: Neostigmine administration after spontaneous recovery to a train-of-four ratio of 0.9 to 1.0: A randomized controlled trial of the effect on neuromuscular and clinical recovery. Anesthesiology 2018; 128:27–37

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Colloids in Major Abdominal Surgery: Are They Really Better?

To the Editor:

With great interest we have read the article by Joosten et al.1 recently published in Anesthesiology. In their study they investigated the use of colloids versus crystalloids in relation to postoperative complications in major abdominal surgery. They conclude that a colloid-based, goal-directed fluid therapy is associated with fewer postoperative complications than a crystalloid-based approach, possibly as a result of a lower intraoperative fluid balance when colloids are used.

In the last decades many studies have focused on hemodynamic optimization in high-risk surgery with fluids, inotropes, and advanced hemodynamic monitoring.2 As protocol adherence remains an issue in most studies, the use of an automated closed-loop system for fluid administration in the study of Joosten et al. is exceptionally elegant. After reading the article we have one major concern: are the groups really comparable? As the authors point out, despite the randomized setup, the baseline characteristics show that surgery duration and anesthesia duration (and hence duration of mechanical ventilation) are both more than an hour longer in the crystalloid group than in the colloid group. No results of statistical tests are provided to verify that the difference is indeed statistically significant, but it is highly likely. Despite the comparable amount of blood loss, the incidence of high-risk surgery, and the Physiological and Operative Severity Score for Enumeration of Mortality and...